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(54) Title: METHOD AND COMPOSITION FOR DISINFECTING CONTACT LENSES

(57) Abstract

Contact lenses are disinfected with solutions comprising about 2 to about 90 ppm of a salt of an N-acyl-L-arginine ester or a derivative thereof. Optional additional ingredients in the solutions include buffer, solute to render the solution isotonic, additional microbicide, and chelating agents. The invention also comprises a method for disinfecting contact lenses with the inventive solutions, as well as tablets, unit doses and kits for forming the solutions.

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METHOD AND COMPOSITION FOR DISINFECTING CONTACT LENSES

INTRODUCTION TO THE INVENTION

Contact lenses have become very popular for correction of defective visual acuity. However, they require a certain amount of care to prevent undesirable side effects, such as infections by various microorganisms which can contaminate the lenses while they are being worn or handled. Accordingly, it is customary to periodically clean the lenses by immersion in a cleaning solution which contains surface active components, disinfecting agents, and other materials.

A disinfectant for soft contact lenses must possess each of the following properties:

(1) it must perform the required disinfection;

(2) it must be harmless to the lenses; and

(3) either:

(a) any amounts remaining on the lens after disinfection must be harmless to the eye of the contact lens wearer; or

(b) it must be capable of being neutralized to a harmless form prior to the wearer's use of the lens.

Three volume percent hydrogen peroxide adequately fulfills the requirements (1), (2) and (3)(b). However, the neutralization step requires that two components be provided and is considered undesirable by many users; it is far more desirable to have a disinfectant that fulfills requirements (1), (2) and (3a). Unfortunately, there are very few known

compositions meeting all of requirements (1), (2) and (3a).

This invention is predicated on the surprising discovery that the use of a specific class of compounds, in a specific concentration range, produces compositions fulfilling all of these requirements. The specific compounds are salts of N-acyl-L-arginine esters and their derivatives, as discussed below. The solutions of the invention are fully compatible with both rigid gas permeable and hydrophilic contact lenses during cleaning, wetting, soaking, rinsing and disinfection.

A technical bulletin (CAE-8301) from Ajinomoto Co., Inc. of Tokyo, Japan, dated 1987 and entitled "Ajinomoto Co., Inc.'s CAE Ethyl N-Cocoyl-L-Arginate PCA Salt" states that the cationic surfactant N-cocoyl-L-arginine ethyl ester, DL-pyrrolidone carboxylic acid salt (called "CAE" by its manufacturer) has marked antibacterial and disinfectant activities, and has a low irritancy to skin and eye mucosa. However, this bulletin gives no indication that CAE may be useful for formulating contact lens disinfecting solutions and would be harmless to contact lenses.

U.S. Patent No. 5,035,859 (Gu et al.), in example 33, discloses a tablet containing 0.75 mg of CAE and 3.75 mg sodium dodecyl sulfate that was dissolved in 7.5 ml of water, thereby creating a solution containing 100 ppm of CAE. However, this example shows a rather poor activity against Candida albicans. Further, this composition has been found to form precipitates after a few days of storage, and damages hydrophilic contact lenses.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a view, partially in cross section, of a container in a kit for practicing the invention.

Fig. 2 is a view of a lens holder cap which can be used with the container of Fig. 1.

SUMMARY OF THE INVENTION

The present invention may be summarized, in part, as a method for disinfecting a contact lens, comprising contacting the lens with an aqueous solution comprising from about 2 to about 90 ppm of a salt of an N-fatty acid acyl-L-arginine ester, or derivative thereof. Solutions, tablets, powders and kits for practicing the method are also included within the invention.

DETAILED DESCRIPTION OF THE INVENTION

The term "ppm" used herein expresses concentration in units of milligrams of a particular component per liter of solution. Unless specified otherwise for a particular value, the term "percent" for a solid composition indicates percentage by weight; for a liquid composition, the term indicates grams per 100 milliliters.

The term "disinfect" means the rendering non-viable of substantially all pathogenic microbes that are in the vegetative state, including gram negative and gram positive bacteria, as well as fungi.

In its broadest aspect, this invention comprises disinfecting contact lenses with aqueous solutions containing from about 2 to about 90 ppm, preferably about 30 to about 70 ppm, of a salt of an N-fatty acid acyl-L-arginine ester (sometimes abbreviated herein as "AAE"), or a derivative thereof. The salts have the following general formula:

$$RCO\text{-}NH\text{-}CH(COOR')\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}NH\text{-}C(NH)(NH_2)\cdot X$$

wherein RCO is the acylation fatty acid moiety and R' is the esterification alcohol moiety. Typically, R will have about 8 to about 20 carbon atoms, in a branched or unbranched configuration. R' typically will have 2 to about 8 carbon atoms. The X in the formula is an acid; this acid can be organic or inorganic (e.g., mineral acids), the choice depending upon the properties required for the molecule.

Especially preferred are AAE compounds wherein RCO is a fatty acid moiety having 10 to about 18 carbon atoms. Representative commercially available salts of N-fatty acid acyl-L-arginine esters have ethyl ester groups and either hydrochloric acid or DL-2-pyrrolidone-5-carboxylic acid (also known as "PCA" or DL-pyroglutamic acid) anions, and are sometimes referred to by the common names of their fatty acid acyl groups:

(a) cocoyl arginine ester (called CAE-PCA);

(b) lauroyl arginine ester (called LAE-PCA or LAE-HCl, depending on the anion present);

(c) myristoyl arginine ester (called MAE-PCA or MAE-HCl, depending on the anion present); and

(d) palmitoyl arginine ester (called PAE-PCA or PAE-HCl, depending on the anion present).

Most of these materials are available from Ajinomoto Co., Inc. in the form of a crystalline powder.

Preparation of the hydrochloride compounds may be accomplished by the procedure of R. Infante et al., in "Surface Active Molecules: Preparation and Properties of Long Chain N-Acyl-L-α-amino-ω-Guanidine Alkyl Acid Derivatives," published in International Journal of Cosmetic Science, Volume 6, pages 275-282, 1984. The PCA salts can be formed using the same procedure, but substituting PCA for the hydrochloric acid.

For the present invention, mixtures of the AAE compounds are very useful. The CAE and MAE compounds can have sufficient antimicrobial activity alone, but

LAE and PAE compounds generally will be used in combination with another AAE compound or another type of microbicide.

Preferably the solution also contains buffer to maintain the solution at pH values about 6 to about 8, more preferably about 6.8 to about 7.8 and most preferably about 7.4. Preferred buffers are borate (e.g., a mixture of boric acid and potassium or sodium borate) and TRIS (tromethamine). Other buffers which are useful include, without limitation, citrate systems (e.g., sodium or potassium citrate and citric acid), sodium bicarbonate, and mixed phosphate buffers containing compounds such as Na_2HPO_4, NaH_2PO_4, K_2HPO_4 and KH_2PO_4. Usually the buffers are present in the disinfecting solution in concentrations of 0.05 to 2.5 percent, preferably 0.1 to 1.5 percent.

Disinfecting solutions in accordance with the invention are preferably isotonic to human tears, i.e., they have an osmolarity of 240 to 330 milliosmoles per kilogram of solution (m Osm/kg). The solutions are rendered isotonic by adding solute, preferably sodium or potassium chloride. The amount of solute to add depends upon the amounts of other ingredients in the solution. For example, if a high concentration of buffer is already present in the solution, less additional solute will be required.

A highly preferred embodiment of the invention involves use of at least one microbicide in addition to the salt of N-fatty acid acyl-L-arginine ester, which has an efficacy-enhancing effect with certain additional microbicides. Preferred additional microbicides include polyhexamethylene biguanide (PHMB), N-(C_8-C_{20}) alkyl-2-pyrrolidone, and chlorhexidine digluconate. Other additional microbicides include alexidine, polyquaternium-1, hexetidine, bronopol, and hydrogen peroxide in very low concentrations, e.g., 50 to 200 ppm. The concentration of additional

microbicid will depend on its identity, the desired speed and completeness of disinfection desired, and the concentration of AAE in the solution. Generally the preferred concentration of the additional microbicide is from 0.5 to 100 ppm.

The inventive solutions will preferably also contain a chelating agent such as amino carboxylic acid compounds or water soluble salts thereof, including ethylenediamine tetraacetic acid (EDTA), nitrilo-triacetic acid, diethylenetriamine pentaacetic acid, hydroxyethyl ethylenediamine triacetic acid, 1,2-diaminocyclohexane tetraacetic acid, ethylene glycol bis(beta-aminoethyl ether)- N,N,N',N'-tetraacetic acid (EGTA), amino diacetic acid and hydroxyethyl amino diacetic acid. These acids can be used in the form of their water soluble salts, particularly their alkali metal salts. Especially preferred chelating agents are the di-, tri- and tetra-sodium salts of ethylene diamine tetraacetic acid, most preferably disodium EDTA (Disodium Edetate).

Other chelating agents such as citrates and polyphosphates can also be used in the present invention. The citrates which can be used in the present invention include citric acid and its mono-, di-, and tri-alkaline metal salts. The polyphosphates which can be used include pyrophosphates, triphosphates, tetraphosphates, trimetaphosphates, tetrametaphosphates, as well as more highly condensed phosphates in the form of the neutral or acidic alkali metal salts such as sodium and potassium salts as well as the ammonium salt.

Solutions in accordance with the present invention may also include surfactants, such as, tyloxapol, which is 4-(1,1,3,3-tetramethylbutyl)phenol polymer with formaldehyde and oxirane; Pluronic® products (available from BASF Corp., Parsippany, New Jersey U.S.A.) or poloxamers, both being nonionic block copolymer

surfactants which are block copolymers of propylene oxide and ethylene oxide; octoxynol or octyphenoxy polyethoxyethanol prepared by reacting isooctylphenol with ethylene oxide; poloxamine which is a block copolymer derivative of ethylene oxide and propylene oxide combined with ethylene diamine; and nonoxynol nonionic surfactant mixtures prepared by reacting nonylphenols with ethylene oxide. It is preferred to use the surfactants which contain an ethylene oxide repeating group. Most of the above surfactants are described in The Merck Index, Eleventh Edition, Merck & Co., Inc., Rahway, New Jersey U.S.A., 1989. The surfactants can be employed in amounts ranging from about 0.0001 to about 20 percent, preferably from about 0.005 to about 5.0 percent, and more preferably from about 0.025 to about 1 percent.

Compositions of this invention may also include viscosity increasing agents to provide lubrication to the eye. Suitable viscosity increasing agents include lecithin or cellulose derivatives such as hydroxymethylcellulose, hydroxypropylcellulose and methylcellulose, usually used in amounts from 0.0001 to 20 percent.

Yet another desirable additional ingredient is one or more enzymes for removing deposits from the lens. Such enzymes include proteases.

Various aspects of the invention include:

(1) the inventive disinfecting solutions,

(2) a method for disinfecting contact lenses with the solutions,

(3) solid compositions, such as tablets or powders, useful for preparing the inventive solutions, and

(4) kits comprising a fixed amount of the solid or a container of the premixed solution, together with a container for conducting the disinfecting.

To prepare the disinfecting solutions, add the solid ingredients to water and agitate until they are completely dissolved. Then adjust the pH of the solution to that desired with, e.g., dilute hydrochloric acid or sodium hydroxide.

To disinfect a contact lens, simply immerse it in the inventive solution for a time sufficient to achieve the desired degree of disinfection. Disinfection time will vary depending upon the concentration of the salt of N-fatty acid acyl-L-arginine ester and the identity and concentration of the other ingredients, and will generally be from 10 minutes to 8 hours. Disinfection may be carried out at room temperature, i.e., about 20° C., but other temperatures are satisfactory and higher temperatures may enhance activity. Lens cleaning is enhanced if, prior to the disinfection, the lenses are rubbed with a few drops of the solution of this invention, saline, saliva or a commercial contact lens cleaner such as PLIAGEL® (a product of Alcon Laboratories Inc., Fort Worth, Texas U.S.A.) and then rinsed with any of those, tap water, etc. to dislodge surface contaminants such as mucous, eye makeup, and the like.

The solid compositions of the invention may include conventional lubricants, binders, and excipients which include, but are not limited to glycerol, sorbitol, propylene glycol, polyethylene glycols and dextran. Highly preferable ingredients in the solid compositions, especially tablets, are a combination of sodium carbonate (or bicarbonate) and adipic acid. This combination acts as a lubricant during the tableting process and renders the tablet effervescent for faster dissolution.

To illustrate the manner in which the invention may be carried out, the following examples are given. It is understood, however, that the examples are for the purposes of illustration and the invention is not

to be regarded as limited to any of the specific materials or conditions set forth therein. The term "q.s." means quantum sufficit or "a sufficient volume" to bring the aqueous solution to specified volume.

The disinfecting efficacy was determined by inoculating the test solution with a microbial suspension at a final concentration of approximately 10^6 colony forming units per ml. Each inoculated solution was then vigorously agitated and kept at ambient temperature. At various times after inoculation each solution was vigorously agitated and 1 ml aliquots withdrawn and dispensed into 9 ml of neutralizing broth. Ten-fold serial dilutions of each inoculated solution were prepared in neutralizing broth. The solutions were plated out at effective dilutions of 1/10th to 1/100,000th on nutrient agar with or without neutralizing agents. The plates were incubated under optimal conditions of time and temperature for growth and the colonies counted.

The concentration of the survivors and the log reductions were calculated. Each ten-fold decrease in microbe concentration constitutes a one-log reduction. In the examples, the following abbreviations apply:

Ingredients

EDTA = Disodium Edetate
LP = N-dodecyl pyrrolidone
PHMB = Polyhexamethylene biguanide
TRIS = Tromethamine
Tyl = Tyloxapol

Microorganisms

S.m. = Serratia marcescens
S.e. = Staphylococcus epidermidis
P.a. = Pseudomonas aeruginosa
C.a. = Candida albicans
A.n. = Aspergillus niger

A.f. = Aspergillus fumigatus

EXAMPLES

The compositions of Examples 1-6 are listed below. The solutions were prepared by dissolving the solid ingredients in water, forming solutions having the indicated percentages (or ppm) of the component.

Example No.	CAE ppm	Boric Acid	Sodium Borate	Sodium Chloride	EDTA	Water
1	50	0.5	0.052	0.66	0	q.s.
2	50	0.5	0.052	0.66	0.1	q.s.
3	50	1.03	0.19	0.3	0.1	q.s.
4	25	1.03	0.2	0.33	0.1	q.s.
5	10	1.03	0.2	0.33	0.1	q.s.
6	5	1.03	0.2	0.33	0.1	q.s.

About 100,000 to 1,000,000 CFU/ml of bacteria were added to above solutions. The surviving cells were determined at periodic time intervals. The results are given below.

	Log Reduction			
	C.a.		S.m.	
Example	1 Hour	4 Hours	1 Hour	4 Hours
1		3.03	>5.06	
2	0.36	0.91	>5.22	
3	0.40	0.75	>6.29	
4			>5.71	
5			3.30	>5.71
6			1.81	2.03

Examples 1 to 6 show that CAE in combination with typical contact lens solution ingredients is an effective disinfectant. Even at a CAE concentration of only 5 ppm, the solution of Example 6 was able to achieve a 100 fold reduction in S. marcescens bacteria,

which is recognized as one of the more difficult organisms to kill.

The following examples illustrate the enhanced effect small amounts of CAE have on an additional microbicide. In this case, the additional microbicide is N-dodecyl-2-pyrrolidone (Surfadone® LP-300, sold by GAF Chemical Corporation, Wayne, New Jersey U.S.A.), the use of which in contact lens disinfection is disclosed in U.S. Patent 5,035,859 to Gu et al. Examples A, B, C and D are provided for comparative purposes.

Solutions

Example No.	LP ppm	CAE ppm	Boric Acid	Sodium Borate	Sodium Chloride	EDTA	Water
A	25	0	0.5	0.052	0.66	0	q.s.
6	25	50	1.03	0.2	0.33	0.1	q.s.
7	25	20	1.03	0.2	0.33	0.1	q.s.
8	25	10	1.03	0.2	0.33	0.1	q.s.
9	25	5	1.03	0.2	0.33	0.1	q.s.
B	20	0	1.03	0.2	0.33	0.1	q.s.
10	20	5	1.03	0.2	0.33	0.1	q.s.
C	10	0	1.03	0.2	0.33	0.1	q.s.
11	10	5	1.03	0.2	0.33	0.1	q.s.
12	10	10	1.03	0.2	0.33	0.1	q.s.
D	5	0	1.03	0.2	0.33	0.1	q.s.
13	5	5	1.03	0.2	0.33	0.1	q.s.

Results

	Log Reduction			
	C.a.		S.m.	
Example	1 Hour	4 Hours	1 Hour	4 hours
A		2.86		1.94
6	>5.46		2.02	>5.37
7			>5.37	

8			>5.37	
9			>5.37	
B	1.92	2.88	0.88	1.08
10	>6.05		4.34	>6.24
C	-0.16	0.47	0.63	0.58
11	4.10	>6.05	4.59	5.49
12	>6.05		>6.34	
D	-0.21	0.03	0.83	2.18
13	3.10	>6.05	>6.34	

The above examples show the enhancement in antimicrobial activity that even small concentrations of CAE can impart to the Surfadone LP-300 solutions.

The following examples 14-19 further illustrate the invention. For comparative example E, OptiFree® (a commercially available contact lens solution sold by Alcon Laboratories Inc.) was used; this solution is described in its package insert as "a sterile, buffered, isotonic, aqueous solution containing a citrate buffer and sodium chloride with edetate disodium 0.05% and POLYQUAD® (polyquaternium-1) 0.001% as preservatives."

Solutions

Example No.	LP ppm	CAE ppm	Boric Acid	Sodium Borate	Chloride	EDTA
14	10	10	1.01	0.19	Isotonic	0.05
15	5	5	1.01	0.19	Isotonic	0.05
16	10	10	1.01	0.19	Isotonic	0.05
17	5	5	1.01	0.19	Isotonic	0.05
18	10	10	1.01	0.19	Isotonic	0
19	5	5	1.01	0.19	Isotonic	0

Results

Example	Log Reduction After 4 Hours	
	S.m.	A.f.
14	>6.2	2.9
15	>6.2	0.9
16	>6.2	1.7
17	4.5	0.5
18	4.1	1.2
19	1.5	0.3
E	2.5	0.1

In the following examples 20-31 and comparative example F, sodium chloride is present in sufficient amounts to render the solutions isotonic.

Example No.	LP ppm	CAE ppm	Boric Acid	Sodium Borate	EDTA	TRIS	Tyl ppm	Log Reduction After 4 Hours C.a.	S.m.	A.f.	P.a.	S.e.
20	10	10	0.50	0.052	0.05	0	0		>6.2	1.7		
21	5	5	0.50	0.052	0.05	0	0		4.5	0.5		
22	10	5	0.50	0.052	0	0	0		4.1	1.2		
23	10	10	1.01	0.19	0.05	0	0		>6.2	2.8		
24	5	5	1.01	0.19	0.05	0	0		>6.2	0.8		
25	10	10	1.01	0.19	0.05	0	0		>6.2	2.9		
26	5	5	1.01	0.19	0.05	0	0		>6.2	0.9		
27	10	10	1.01	0.19	0.05	0	0	1.1			>6.0	4.3
28	0	10	0	0	0.05	1.2	0		4.4			
29	10	10	0	0	0.05	1.2	0		>6.7			
30	5	5	0	0	0.05	1.2	0		1.1	0.4		
31	10	12.5	0	0	0.05	1.2	10	5.3	4.4			
F	10	0	0	0	0.05	1.2	10	1.9	0.5			

Experiments are conducted to show the effects of combining the AAE salts with small amounts of disinfectants used for contact lenses. In each comparison group, the base solution is constant and only the concentrations and identity of two disinfectants is varied; base solutions may be different for each of the comparisons. The numeric values below are log reductions in microorganism counts after the indicated times. The "Mixed" disinfectant is formed by combining 1 part by weight of MAE-PCA with 4 parts by weight of LAE-PCA.

	C.a.		S.m.	
Disinfectant	1 hour	4 Hours	1 Hour	4 Hours
CAE, 50 ppm		3.0		>5
Bronopol, 50 ppm		1.55		0.67
CAE + Bronopol, 50 ppm total		>5		>6
CAE + Bronopol, 20 ppm total		>5.8		>6
CAE + Bronopol, 10 ppm total		2.1		>6
CAE, 10 ppm		0.2		1.8
CAE, 25 ppm		0.2		1.0
CAE, 10 ppm + PHMB, 1.5 ppm		1.7		>5.8
CAE, 25 ppm + PHMB, 1.5 ppm		2.2		>5.8
CAE, 10 ppm		<1	3.3	>5.7
Hexetidine, 10 ppm	2.7	>5.3		<1
CAE, 25 ppm		0.4	>5.7	>5.7
CAE, 10 ppm + Hexetidine, 10 ppm	>6.2	>6.2	>5.7	>5.7

Mixed, 50 ppm	2.1	2.2	>6.3	>6.3
Alexidine, 50 ppm	>6.2	>6.2	>6.3	>6.3
Mixed, 40 ppm + Alexidine, 10 ppm	2.1	3.7	>6.3	>6.3
Mixed, 25 ppm + Alexidine, 25 ppm	4.7	>6.2	>6.3	>6.3
Mixed, 10 ppm + Alexidine, 40 ppm	>6.2	>6.2	>6.3	>6.3

An aqueous solution containing a mixture of AAE compounds is prepared, using the following components (concentrations in percent, unless other units are given) and adjusting the final pH to about 7.4:

Component	Amount
Sodium borate	0.2
Boric acid	1.0
Sodium chloride	0.3
Triton® X-100	150 ppm
Triton® X-400	175 ppm
MAE-PCA	10 ppm
LAE-PCA	40 ppm
EDTA	0.1

The Triton® components are sold by Rohm and Haas Co., Philadelphia, Pennsylvania U.S.A. and are octylphenoxy polyethoxy ethanols. The X-100 is thought to have an average of about 9 ethoxy groups per molecule, while the X-400 has an average of about 40 ethoxy groups.

Effectiveness of this solution against various microorganisms is shown in the following table:

	Log Reduction	
Microorganism	2 Hours	4 Hours
S.m.	4.69	6.34
S.e.	5.17	6.36

P.a.		6.10
C.a.	2.18	4.45
A.n.	1.18	2.93

Two useful effervescent tablet formulations for disinfecting contact lenses contain the following ingredients, where the values are expressed in milligrams:

	Tablet	
Component	A	B
CAE	0.5	0.5
EDTA	0	1
Adipic acid	27	0
Tartaric acid	0	27
Sodium carbonate	28	28

To prepare the tablets, thoroughly crush the ingredients to a powder which will pass through a 200 mesh sieve, blend thoroughly in the correct proportion and press into tablets with a standard tablet press. The tablets above are intended for dissolution in 7.5 ml of normal saline solution. These formulations can be adjusted for use with tap water (e.g., by adding sodium chloride) or for different amounts of liquid.

Tablets provide enhanced long-term storage stability and user convenience. The tablets, for maximum ease of storing and carrying, can be packaged in the well-known foil backed "blister packs," and dispensed singly as needed. As an alternative to tablets, the powdered components may be blended and appropriate unit amounts sealed into pouches or envelopes, for opening by a user at the time of solution preparation; frequently these powder formulations will dissolve readily in aqueous media and do not need to contain gas-forming components.

One embodiment of a kit for cleaning contact lenses is shown, in part, in Figs. 1 and 2. Bottle **10** is used to contain the cleaning solution, and is provided with internal ring **12** which indicates the desired liquid filling level. External threads **14** are provided at the top of the bottle. The lens holder cap assembly **16** has internal threading **18** for attachment to the bottle by engagement with the external threads thereon, and an extending platform **20**. Hinged lens covers **22** and **24** are mounted onto opposite sides of the platform and can be secured to the platform to retain contact lenses during a cleaning procedure. The platform and lens covers are typically perforated or slotted in appropriate areas to allow free access of disinfecting solution to all surfaces of the lenses. Frequently one or both of the covers will be marked to indicate which lens came from the user's left (and/or right) eye.

To use the kit, a user places a tablet or powder disinfecting agent (not shown), which is typically supplied in the kit, into the empty bottle, then fills the bottle to the level of the internal ring with water, saline solution or other specified liquid. If effervescent tablets are not used, the bottle may require shaking or swirling with the cap installed, to insure complete dissolution of the solid agents. Alternatively, the user simply fills the bottle to the indicating ring with pre-prepared disinfecting solution (not shown), typically provided in the kit.

Lenses are installed between the hinged covers and the platform, and the cap is threaded onto the bottle to submerge the lenses in disinfecting solution for a prescribed time. After the procedure, the bottle is emptied and rinsed to remove residual solution.

The invention has been described with respect to several specific embodiments, but is not to be limited

thereto. Further embodiments and modifications will be apparent to those skilled in the art and are included within the invention, the scope of the invention being defined solely by the appended claims.

WHAT IS CLAIMED IS:

1. A method for disinfecting a contact lens comprising contacting the lens with an aqueous solution comprising about 2 to about 90 ppm of a salt of an N-acyl-L-arginine ester or a derivative thereof.

2. The method of claim 1 wherein the concentration of ester or its derivative is about 30 to about 70 ppm.

3. The method of claim 1 wherein the solution further comprises a buffer to maintain the solution in the pH range of about 6 to about 8.

4. The method of claim 3 wherein the solution further comprises solute in amounts to make the solution isotonic.

5. The method of claim 1 wherein the solution further comprises at least one additional microbicide.

6. The method of claim 3 wherein the solution further comprises at least one additional microbicide.

7. The method of claim 4 wherein the solution further comprises at least one additional microbicide.

8. The method of claim 1 wherein the solution further comprises a chelating agent.

9. The method of claim 4 wherein the solution further comprises a chelating agent.

10. The method of claim 7 wherein the solution further comprises a chelating agent.

11. The method of claim 1 wherein the solution further comprises an additional surfactant.

12. An aqueous contact lens disinfecting solution comprising:

(a) about 2 to about 90 ppm of a salt of an N-acyl-L-arginine ester or a derivative thereof;

(b) sufficient buffer to maintain pH in the range of about 6 to about 8; and

(c) sufficient solute to render the solution isotonic.

13. The solution of claim 12 further comprising an additional microbicide.

14. The solution of claim 12 further comprising a chelating agent.

15. The solution of claim 12 further comprising an additional surfactant.

16. The solution of claim 12 wherein the buffer is selected from a borate buffer and tromethamine, and the solute is sodium or potassium chloride.

17. The solution of claim 13 wherein the additional microbicide is selected from PHMB and N-(C_8-C_{20})-alkyl-2-pyrrolidone.

18. The solution of claim 14 wherein the chelant is disodium EDTA.

19. The solution of claim 15 wherein the additional surfactant contains ethylene oxide-derived repeating groups.

20. The solution of claim 12 wherein (b) is a borate buffer, the solution further containing:

(d) an additional surfactant containing ethylene oxide-derived repeating groups; and

(e) a chelant.

21. The solution of claim 20, wherein the additional surfactant is a mixture of octylphenoxy polyethoxy ethanols.

22. The solution of claim 20, wherein the chelant is a salt of ethylenediamine tetraacetic acid.

23. The solution of claim 20, wherein the salt of (a) is a mixture of DL-2-pyrrolidone-5-carboxylic acid salts of N-lauroyl-L-arginine ethyl ester and N-myristoyl-L-arginine ethyl ester.

24. A tablet or other unit dose for dissolution in a specified volume of aqueous liquid, comprising a salt of an N-acyl-L-arginine ester or derivative thereof, and an ophthalmologically acceptable carrier, the salt being present in the aqueous liquid at about 2 to about 90 ppm following dissolution.

25. A kit for disinfecting a contact lens comprising at least one tablet or other unit dose in accordance with claim 24 and a container calibrated to hold the specified amount of liquid.

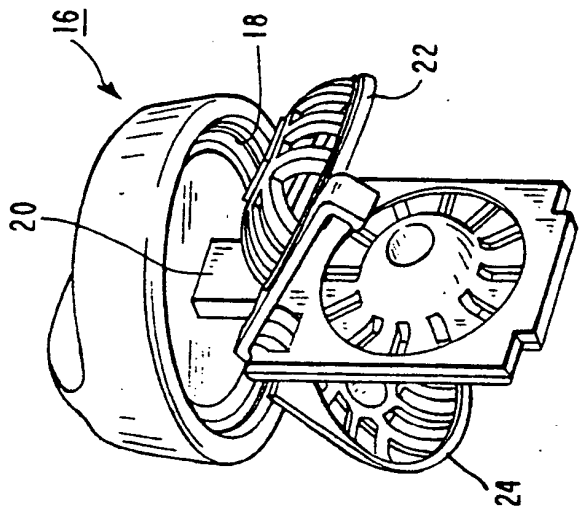

FIG. 2

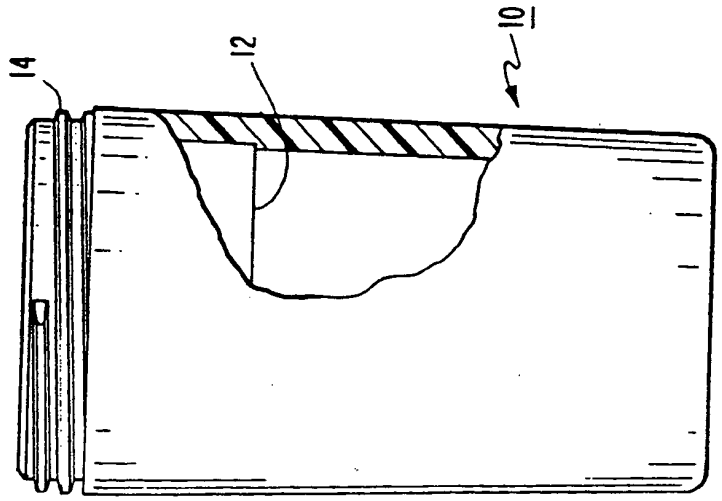

FIG. 1

INTERNATIONAL SEARCH REPORT

Inte ɔnal Application No
PCT/US 94/01607

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61L2/18 G02C13/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO,A,91 07192 (SCHERING) 30 May 1991 see page 14, line 33 - line 34; example 33 see page 15, line 1 - line 2; claim 10	1-25

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
4 May 1994	18. 05. 94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Peltre, C

Form PCT/ISA/210 (second sheet) (July 1992)

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WO-A-9107192	30-05-91	US-A-	5035859	30-07-91
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		AU-A-	6879691	13-06-91
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